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(54) [Title of the Invention] REMEDY FOR HYPERLIPIDEMIA

(57) [Abstract]

[Problem to be Solved]

A new remedy for hyperlipidemia and a health food containing the same are provided.

[Solution]

A pine bark extract is used as a remedy for hyperlipidemia. A preferable pine bark extract contains 20 wt% or more of OPC (oligomeric proanthocyanidin) and 5.0 wt% or more of catechins. A food containing this pine bark extract and ascorbic acid or a salt thereof has an excellent effect of improving hyperlipidemia and can decrease blood levels of total cholesterol, LDL cholesterol, neutral lipid, and phospholipid and simultaneously increase a blood HDL cholesterol level.

[Claims for the Patent]

[Claim 1]

A remedy for hyperlipidemia characterized by containing a pine bark extract.

[Claim 2]

The remedy for hyperlipidemia according to claim 1, wherein the pine bark extract contains 20 wt% or more of OPC (oligomeric proanthocyanidin).

[Claim 3]

The remedy for hyperlipidemia according to claim 2, wherein the pine bark extract further contains 5.0 wt% or more of catechins.

[Claim 4]

The remedy for hyperlipidemia according to any one of claims 1 to 3, further containing ascorbic acid or a salt thereof.

[Claim 5]

A health food containing a remedy for hyperlipidemia according to any one of claims 1 to 4.

[Detailed Description of the Invention]

[0001]

[Field of the Invention]

The present invention relates to a remedy for hyperlipidemia characterized by containing a pine bark extract and relates to a health food containing the same.

[0002]

[Conventional Art]

Recently, the number of patients suffering from so-called lifestyle-related diseases such as hyperlipidemia and diabetes

mellitus has increased due to changes in diets. In particular, hyperlipidemia keeps a blood lipid level high and develops into arteriosclerosis, hypertension, cerebral apoplexy, or the like as it progresses and therefore should be paid careful attention. Mainly, two kinds of lipid, cholesterol and neutral lipid, are present in blood. Cholesterol is classified into LDL (low-density lipoprotein) and HDL (high-density lipoprotein). In the two, LDL becomes a cause of the aforementioned lifestyle-related diseases and thereby is called "bad" cholesterol. On the other hand, HDL has an activity of removing free cholesterol that can be a cause of arteriosclerosis or the like and is thereby called "good" cholesterol.

[0003]

Accordingly, investigation on improvement of hyperlipidemia has been conducted by entirely focusing on the removal of LDL. However, recently, it has been also revealed that hyperlipidemia can be improved by increasing the ratio of HDL in total cholesterol, even if the total cholesterol concentration does not decrease. Therefore, the ratio of HDL in total cholesterol can be an indicator of improvement of hyperlipidemia.

[0004]

Naturally, a drug is used for improving such hyperlipidemia. However, improvement of hyperlipidemia can be easily attempted if intake of a food is effective. It has been reported that vitamin C (ascorbic acid) in foods has an activity to decrease blood cholesterol levels. Vitamin C is a micronutrient essential to human life and also has an immunostimulating activity and skin whitening/beautifying activity.

[0005]

However, vitamin C is a water-soluble vitamin, cannot remain in vivo for a long time, and is usually excreted into the urine within two or three hours after the intake. Therefore, the activity of decreasing blood cholesterol levels is insufficient. In order to sufficiently exhibit the activity of decreasing blood cholesterol levels, it is required, for example, that the daily dosage of vitamin C is dividedly ingested every several hours. Thus, it is very complicated.

[0006]

Accordingly, foods that can improve hyperlipidemia are required.

[0007]

[Problems to be Solved by the Invention]

The present invention has been made in view of the above-mentioned circumstances, and an object of the present invention is to provide a new remedy for hyperlipidemia and a health food containing the same.

[0008]

[Means for Solving the Problems]

The present inventors have searched natural products that can improve hyperlipidemia and, as a result, have found that a pine bark extract has an effect of improving hyperlipidemia. Furthermore, the present inventors have found that hyperlipidemia is improved by using the pine bark extract in combination with ascorbic acid or a salt thereof. Thus, the present invention has been accomplished.

[0009]

That is, the present invention provides a remedy for hyperlipidemia containing a pine bark extract.

[0010]

In a preferable embodiment, the pine bark extract contains 20 wt% or more OPC (oligomeric proanthocyanidin).

[0011]

Furthermore, in a preferable embodiment, the pine bark extract contains 5.0 wt% or more of catechins in addition to OPC.

[0012]

Furthermore, in a preferable embodiment, the remedy for hyperlipidemia further contains ascorbic acid or a salt thereof.

[0013]

Furthermore, the present invention provides a health food containing any of the aforementioned remedies for hyperlipidemia.

[0014]

Hyperlipidemia can be improved on a daily basis by ingesting a remedy for hyperlipidemia containing a pine bark extract or a health food containing the remedy for hyperlipidemia, according to the present invention.

[0015]

[Embodiments of the Invention]

The remedy for hyperlipidemia of the present invention is characterized by containing a pine bark extract. Examples of the pine bark extract preferably include bark extracts of Pinus Martima, Larix kaempferi (Lamb.) Carr., Pinus thunbergii Parl., Pinus densiflora Sieb. et Zucc., Pinus parviflora, Pinus parviflora Sieb. et Zucc., Pinus koraiensis Sieb. et Zucc., Pinus pumila (Pall.) Regel, Pinus luchuensis Mayr, Pinus

densiflora form. Umbraculifera, Pinus palustris, Pinus bungeana, and Aneda, which is found in the province of Quebec, Canada. Among them, a bark extract of Pinus Martima is preferably used.

[0016]

Pinus Martima is a maritime pine growing in a part of Atlantic Ocean coast of the south France. The bark of this Pinus Martima contains proanthocyanidin, one of flavonoids, as the main component and also organic acids and other physiologically active components. This main component, proanthocyanidin, is known to have a strong antioxidative activity for eliminating active oxygen.

[0017]

The pine bark extract is obtained by extracting the aforementioned pine bark with water or an organic solvent. The water used in the extraction is warm water or hot water. The organic solvent used in the extraction is preferably one that is acceptable for manufacturing foods or drugs, such as methanol, ethanol, 1-propanol, 2-propanol, 1-butanol, 2-butanol, butane, acetone, hexane, cyclohexane, propylene glycol, water-containing ethanol, water-containing propylene glycol, ethyl methyl ketone, glycerin, methyl acetate, ethyl acetate, diethyl ether, dichloromethane, edible oil and fat, 1,1,2,2-tetrafluoroethane, and 1,1,2-trichloroethene. These water and organic solvents may be used alone or as a combination thereof. In particular, hot water, water-containing ethanol, and water-containing propylene glycol and the like are preferred.

[0018]

Any method may be used for the extraction from pine bark without particular limitation, and examples thereof include a heating extraction method and a supercritical fluid extraction method.

[0019]

The supercritical fluid extraction method uses a supercritical fluid, which is a fluid in a state exceeding the critical point (critical temperature or critical pressure) of vapor-liquid transition of a substance, and, for example, carbon dioxide, ethylene, propane, or nitrous oxide (laughing gas) is used as the supercritical fluid. Carbon dioxide is preferred.

[0020]

The supercritical fluid extraction method includes an extraction step extracting a target component with a supercritical fluid and a separation step separating the target component from the supercritical fluid. The separation step may be conducted by any of the following: selective extraction by changing pressure, selective extraction by changing temperature, or selective extraction by using an adsorbent or an absorbent.

[0021]

Furthermore, the supercritical fluid extraction may be conducted by an entrainer addition method. In this method, the extraction fluid is mixed with about 2 to 20 w/v% of ethanol, propanol, n-hexane, acetone, toluene, other aliphatic lower alcohol, aliphatic hydrocarbon, aromatic hydrocarbon, ketone, or the like, and this fluid is used for the supercritical fluid extraction. With this, the solubility of a target extract, such as OPC or catechins, in an extraction solvent is remarkably

increased, or the selectivity of separation is improved. Thus, the method can efficiently give a pine bark extract.

[0022]

Since the supercritical fluid extraction method can be conducted at a relatively low temperature, there are advantages that it can be applied to a material that is deteriorated or decomposed at high temperature and that the extraction fluid does not remain. In addition, since cyclic use of a solvent is possible, a process of removing the solvent is unnecessary to advantageously simplify the process.

[0023]

In addition to the above-described methods, the extraction from pine bark may be performed by a batch method using liquid carbon dioxide, a reflux method using liquid carbon dioxide, a reflux method using supercritical carbon dioxide, or the like.

[0024]

Furthermore, the extraction from pine bark may be conducted by a combination of a plurality of extraction methods. The extraction by a combination of a plurality of extraction methods enables to obtain pine bark extracts containing various compositions.

[0025]

The pine bark extract used in the present invention contains condensation polymers of proanthocyanidin, namely, condensation polymers having a constitution unit of flavan-3-ol and/or flavan-3,4-diol and having a polymerization degree of 2 or more. Condensation polymers having a low polymerization degree are preferred. The polymerization degree of the condensation

polymers is preferably 2 to 30 (dimer to 30 mer), more preferably 2 to 10 (dimer to decamer), and most preferably 2 to 4 (dimer to tetramer).

[0026]

In the present invention, among condensation polymers of proanthocyanidin, a condensation polymer having a constitution unit of flavan-3-ol and/or flavan-3,4-diol and having a polymerization degree of 2 or more is referred to as OPC (oligomeric proanthocyanidin).

[0027]

OPC is a kind of polyphenol and is a strong antioxidative substance produced in plants, and it is abundantly contained in leaves and barks of plants, and rinds or seeds of fruits. Specifically, OPC is contained in seed of grape, pine bark, inner skin of peanut, ginkgo, fruit of false acacia, cowberry, and the like. Furthermore, it is known that OPC is contained in cola nuts of West Africa, root of Rathania of Peru, and green tea of Japan. OPC is a substance that cannot be produced in the human body.

[0028]

Such OPC is an antioxidative substance and therefore has an effect of reducing a risk of lifestyle-related diseases such as cancer, heart disease, and cerebral thrombosis and an effect of improving allergic diathesis such as arthritis, atopic dermatitis, and hay fever.

[0029]

Furthermore, it is known that, in addition to the antioxidative activity, OPC has effects of suppressing

proliferation of bacteria in the mouth to decrease dental plaques, retrieving elasticity of blood vessels, preventing lipoprotein in blood from damage caused by active oxygen so that aggregation of damaged fat onto the inner walls of blood vessels and adhesion of cholesterol thereto are prevented, reproducing vitamin E decomposed by active oxygen, enhancing vitamin E activity, and so on.

[0030]

In the present invention, a pine bark extract preferably contains 20 wt% or more of OPC and more preferably 30 wt% or more.

[0031]

A pine bark extract containing OPC can achieve more excellent effects of preventing and treating hyperlipidemia compared to that containing a condensation polymer of a higher polymerization degree.

[0032]

The pine bark extract used in the present invention preferably contains 5 wt% or more of catechins. Catechins are extracted from a pine bark too and is contained in a pine bark extract. That is, catechins can be extracted together with OPC.

[0033]

The term catechins is a collective designation of polyhydroxyflavan-3-ol. In addition to (+)-catechin that is called catechin in a narrow sense, gallocatechin, afzelechin, and 3-galloyl derivatives of (+)-catechin and gallocatechin are isolated from natural products. As catechins, for example, (+)-catechin, (-)-epicatechin, (+)-gallocatechin, (-)-

epigallocatechin, epigallocatechin gallate, and epicatechin gallate are known. Catechins are known to have activities of inhibiting cancer, preventing arteriosclerosis, inhibiting fat metabolism disorders, inhibiting an increase in a blood pressure level, and preventing blood clots, anti-allergy, anti-virus, and antibacterial activities, and activities of preventing dental caries, preventing foul breath, and normalizing intestinal bacterial flora, effects of eliminating active oxygen and free radicals, an antioxidative effect, and so on. In addition, catechins are known to have an antidiabetic effect of inhibiting an increase in blood sugar level.

[0034]

Catechins have properties to be readily dissolved in water in the presence of OPC and, simultaneously, be activated.

[0035]

The remedy for hyperlipidemia according to the present invention most preferably use a pine bark extract containing 5 wt% or more of catechins and 20 wt% or more of OPC. When the OPC content in a pine bark extract is less than 20 wt% or the catechins content is less than 5 wt%, OPC or catechins may be added to the pine bark extract so that the OPC content becomes 20 wt% or more or the catechins content becomes 5 wt% or more.

[0036]

The pine bark extract used in the remedy for hyperlipidemia according to the present invention is specifically prepared by the following method. However, the method is an exemplary example, and the present invention is not limited thereto.

[0037]

One kilogram of a bark of Pinus Martima is extracted with 3 L of a sodium chloride saturated solution at 100°C for 30 minutes to give an extract (extraction process). Then, the extract is filtered, and the resulting insoluble materials are washed with 500 mL of a sodium chloride saturated solution to collect the wash solution (washing process). The extract and the wash solution are combined as a crude extract of the pine bark. [0038]

Then, this crude extract is subjected to an ethyl acetate layer collecting process by adding 250 mL of ethyl acetate to the crude extract for phase separation and collecting the ethyl acetate layer. This process is repeated five times. In this ethyl acetate layer collecting process, the ethyl acetate layer is dehydrated with 200 g of anhydrous sodium sulfate and is recovered. Then, this ethyl acetate layer is filtered, and the filtrate is concentrated under reduced pressure to a volume of one-fifth of the original. The concentrated ethyl acetate layer is poured into 2 L of chloroform, followed by stirring. The resulting precipitate is collected by filtration. Then, this precipitate is dissolved in 100 mL of ethyl acetate, and the mixture is added to 1 L of chloroform again to give a precipitate. This process is repeated twice as a washing process. This method gives about 5 g of a pine bark extract containing 20 wt% of OPC of dimer to tetramer and 5 wt% or more of catechins. [0039]

In order to achieve the effect as a remedy for hyperlipidemia of the present invention, it is preferable that the pine bark extract be administered or ingested to a human in

a total dose per day of 50 to 2000 mg and preferably 100 to 1000 mg.

[0040]

The health food of the present invention is prepared by blending the pine bark extract with a food. The content of the pine bark extract in the health food may be determined in consideration of the above-mentioned intake.

[0041]

The health food of the present invention may be mixed with additional substances such as an excipient, a filler, a binder, a thickener, an emulsifier, a coloring agent, a flavoring agent, a food additive, and seasoning, according to need. For example, royal jelly, vitamin, protein, calcium such as egg shell, chitosan, lecithin, chlorella powder, Angelica keiskei powder, Corchorus capsularis powder, or the like can be admixed as nutrition supplements. Furthermore, stevia powder, powdered green tea, lemon powder, honey, hydrogenated maltose, lactose, a sugar solution, seasoning, or the like can be added to improve flavor.

[0042]

The food can be made in the form of a capsule such as a hard capsule and a soft capsule, a tablet, or a pill, or can be powder, granules, or candy-shaped, according to need.

[0043]

The amount of pine bark extract contained in such a health food varies depending on the formulation and is in the range of 0.5 to 10 wt% and preferably 1 to 7 wt%.

[0044]

The remedy for hyperlipidemia and the health food containing the same according to this embodiment may be ingested directly or may be drunk by dissolving them in water, hot water, milk, or the like or may be drunk as the components percolated, according to the shape or taste.

[0045]

[Example]

The present invention will now be described with reference to an example, but is not limited this example.

[0046]

(Example) Effect of a remedy for hyperlipidemia of the present invention was evaluated as described below by using purified feed containing L-ascorbic acid at a low concentration and a pine bark extract containing 20 wt% of OPC and 5 wt% or more of catechin (hereinafter simply referred to as pine bark extract) prepared by the above-described method.

[0047]

Three-week old male guinea pigs (Japan SLC) were fed with usual solid feed (RC4, Oriental Yeast) for one week for habituation, and then separated into groups each consisting of seven guinea pigs by a randomized method.

[0048]

Purified feed containing L-ascorbic acid (0.01 wt%) was prepared. This purified feed had a composition of cornstarch (29.49%), milk casein (20.00%), alfalfa meal (10.00%), α-potato starch (10.00%), cellulose powder (10.00%), sucrose (10.00%), soybean oil (6.00%), a mineral mixture (AIN-76, 3.50%), a

vitamin mixture (AIN-76, 1.00%), and ascorbic acid (0.01%). All numbers indicate wt%.

[0049]

Then, this purified feed was mixed with the pine bark extract so as to contain 2.5 wt% of the extract, and the mixture was formed into solid feed. This solid feed was freely ingested by the guinea pigs for 28 days.

[0050]

After the administration for 28 days, blood cholesterol levels, LDL cholesterol levels, HDL cholesterol levels, triglyceride concentrations, and phospholipid concentrations were measured using a measurement kit.

[0051]

The unit of each value and the measurement method are as follows:

(1) Total cholesterol: mg/dL, enzyme method ("Serotec" TCHO-L: Serotec)

(2) LDL cholesterol: mg/dL, enzyme method ("Choles Test LDL": Daiichi Pure Chemicals)

(3) HDL cholesterol: mg/dL, enzyme method ("Choles Test HDL": Daiichi Pure Chemicals)

(4) Triglyceride: mg/dL, enzyme method ("Serotec" TG-L: Serotec)

(5) Phospholipid: mg/dL, enzyme method ("Serotec" PL-L: Serotec)

[0052]

Table 1 shows the results. In Table 1, the control shows values of a group in which guinea pigs were fed with purified feed not containing the pine bark extract.

[0053]

[Table 1]

	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglyceride	Phospholipid
Control group	42.6±4.2	29.3±3.8	4.1±0.4	48.3±6.6	32.9±2.5
Example group	33.0±2.6	21.1±2.5	5.1±0.5	28.4±3.2	26.8±1.6
Rate of change (%)	-22.5	-28.0	24.4	-41.2	-18.5

[0054]

The results shown in Table 1 confirm that the remedy for hyperlipidemia containing ascorbic acid and a pine bark extract of the present invention decreases a total cholesterol level, an LDL cholesterol level, and a triglyceride (neutral lipid) concentration by 22.5%, 28.0%, and 41.2%, respectively, and, at the same time, increases an HDL cholesterol level, which is known as good cholesterol, by 24.4%. Thus, the remedy for hyperlipidemia is shown to be useful for improving hyperlipidemia.

[0055]

[Advantages of the Invention]

According to the present invention, a remedy for hyperlipidemia containing a pine bark extract is provided. In particular, the use of a remedy for hyperlipidemia containing ascorbic acid or a salt thereof, 20 wt% or more of OPC, and 5 wt% or more of catechin can decrease blood total cholesterol, LDL cholesterol, neutral lipid, and phospholipid levels and can simultaneously increase an HDL cholesterol level.